What's So 'New' About New Psychoactive Substances? Definitions, prevalence, motivations, user groups and a proposed new taxonomy

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Abstract

This chapter provides an overview of the varied definitions of New Psychoactive Substances (NPS) or so-called 'legal highs', along with data on (relatively low) prevalence in selected countries and user motivations in order to tease out the broader picture of what characterises NPS use. A new typology of NPS is proposed which couples pharmacological effects with chemical classifications, to provide an underlying framework for this review. The authors conclude that the dynamic interaction between the NPS market and policy change initially characterised as 'cat and mouse' might now be conceived of as 'hare and hounds' in that legislative control has been a significant driving force in manufacturing and retail innovations

Author Bio

Fiona Measham was appointed Professor of Criminology at Durham University in 2013. Fiona has conducted research for over two decades exploring changing trends in legal and illegal drugs; the night time economy and the socio-cultural context to consumption; New Psychoactive Substances and broader policy implications. Fiona was appointed to the Advisory Council on the Misuse of Drugs in 2009: currently she is Chair of the ACMD Polysubstance Use Working Group and Mephedrone review sub-group, and sits on the New Psychoactive Substances standing committee and NPS Watch List sub-group. Fiona was appointed to the Home Office Ministerial Expert Panel on New Psychoactive Substances in 2014 and Public Health England's Drug Treatment Expert Reference Group in 2015.

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Keywords

New Psychoactive Substances, NPS, legal highs, definitions, prevalence, motivations

Introduction

One of the most interesting developments in the field of drug and alcohol studies in recent years has been the emergence of New Psychoactive Substances (NPS). This phenomenon is something of a (rapidly) moving target however, in terms of what we know about NPS, how different countries have reacted to their emergence and indeed, what we even mean by the term. This chapter will explore definitions, prevalence and user motivations in order to tease out the broader picture of what characterises NPS use, such that it should warrant a chapter in and of itself in this collection. A new typology of NPS is also proposed here, which couples pharmacological effects with chemical classifications, to provide an underlying framework for this review.

Although prevalence of use of NPS remains low by comparison with both established illegal drugs such as cannabis and cocaine, and established legal drugs such as alcohol and tobacco, this chapter suggests that the significance of the interest generated by NPS relates to the rapidity of innovation in manufacturing and retail practices; the speed and scale of policy responses; and the relationship between the two, which was initially characterised by commentators as 'cat and mouse'.[1] The authors conclude here that the dynamic interaction between the NPS market and policy change can be better characterised as 'hare and hounds' in that legislative control has been a significant driving force in manufacturing and retail innovations.

Definitions

The emergence and evolution of the NPS issue parallels the emergence and evolution of the terminology used to describe the appearance of a cluster of psychoactive substances in recent years which, unusually for the drugs field, were identified as a potential global threat *before* a significant physical or social problem emerged. The roots of the NPS debate can be traced back to the 1970s and the development of the term 'designer drug', itself a somewhat imprecise term, used to characterise psychoactive substances that were

[1] Another metaphor applied to the relationship between pharmacological entrepreneurship and NPS legislative control compares this dynamic with 'cutting off the hydra's head' where several more grow back in its place, eg. '*Drugs have been a problem for centuries but legal highs have turned them into a narcotics version of Lernaean Hydra'* (http://www.telegraph.co.uk/men/active/mens-health/11310863/Why-the-problem-of-legal-highs-wont-go-away.html)

derivatives of controlled drugs and had been created to circumvent existing legal restrictions specifically for recreational purposes. Buchanan and Brown (1988), who ascribe the coining of the term to a California pharmacologist called Henderson, identify four main categories of 'designer drugs': phenylethylamines (eg. MDMA), synthetic opioids, methaqualone derivatives and arylhexylamines (eg. phencyclidine or PCP also known as 'Angel Dust', perhaps the most highly publicised of the 1970s designer drugs in the United States). However, contrary to the implication that these substances were created by street chemists, in fact many of these 'designer drugs' were the offshoots or rejects of commercial pharmaceutical research and development and hence the details of their synthesis had already been published in professional and academic papers (see Brandt et al., 2014 for an overview of the development of NPS nomenclature and definitions). Whilst the term 'designer drugs' continued to be used throughout the 1980s and 90s, another term started to emerge – 'legal highs' – which was an indication of the broadening array of herbal as well as synthetic substances available as pills, powders, liquids and vegetable matter that were being manufactured and sold to emulate the appearance and effects of existing recreational drugs and to evade legislative control. The shift in emphasis here was towards herbal, and therefore by implication 'natural', products ('herbal highs') in contrast to the 'synthetic' associations of 'designer drugs' (also known as 'research chemicals').

In terms of NPS specifically, the watershed moment came in 2008 when the manufacture of synthetic cannabinoids and substituted cathinones became an international concern. Such were the numbers of new psychoactive substances identified by forensic scientists around the world from 2008 onwards that the term Novel Psychoactive Substances (Dargan et al., 2013) or New Psychoactive Substances was coined (EMCDDA, 2007). For example, the term was widely enough accepted in scientific circles that by 2009 the UK Advisory Council on the Misuse of Drugs (ACMD) established a "New Psychoactive Substances Working Group" to address concerns.[2] The definition utilised by the ACMD working group was: "Psychoactive drugs which are not prohibited by the United Nations Single Convention on Narcotic Drugs or by the Misuse of Drugs Act 1971, and which people in the UK are seeking for intoxicant use." (ACMD, 2011: 10.)

[2] 8th October 2009, Measham in attendance.

Similarly the definition utilised by the UK Association of Chief Police Officers (ACPO) at this time also emphasised legal status – specifically the lack of legislative control within the UK – as the defining feature in its definition: "New Psychoactive Substances or so called 'legal highs' are substances which produce the same, or similar effects, to illegal stimulant drugs such as cocaine and ecstasy, but are not controlled under legislation [the Misuse of Drugs Act 1971 in the UK]. They are however, considered illegal under current medicines legislation to sell, supply or advertise for 'human consumption'" (ACPO, 2011: 19). This emphasis on circumventing legislative control led Newcombe to suggest that 'legal highs', the term still favoured by the media and in everyday conversation, could more accurately be considered "legal loophole" drugs (Newcombe, 2012a). Most recently the acronym NPS has increasingly emphasised *New* Psychoactive Substances (eg. NPS Review Expert Panel, 2014) rather than *Novel* Psychoactive Substances (eg. ACMD, 2011; Dargan et al., 2013), in recognition that whilst their *recreational* use might be a relatively recent concern, the drugs themselves were not necessarily novel in that at least some of them had an established, if not unproblematic, history of pharmaceutical development.

The United Nations Office on Drugs and Crime (UNODC) has clarified the meaning of 'new' in their definition of NPS: "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat. The term 'new' does not necessarily refer to new inventions – several NPS were first synthesized 40 years ago – but to substances that have recently emerged on the market and which have not been scheduled under the above Conventions" (UNODC, 2013: 2). Other variations in the NPS literature include 'emerging' in place of 'novel' or 'new' and 'compounds' or 'drugs' instead of the more general term 'substances'.

The definition and scope of NPS continues to evolve and expand to include both controlled and uncontrolled psychoactive drugs, synthetic and natural substances, as well as substances that are inadvertently consumed as adulterants or substitutes to the drug of choice.[3] With so much emphasis placed on defining, identifying and cataloguing new NPS

[3] Two examples of these are firstly, BZP which was mis-sold as ecstasy in the UK in 2009/10 and appeared widely in forensic analyses of police seizures but had negligible reported use in general population surveys (Hoare and Moon, 2010) and self report surveys (Measham et al., 2011a; Measham et al., 2011) at that time. PMA/PMMA was banned under UK generic legislation in 1977 and has been mis-sold as ecstasy, particularly

through national and international warning systems (EMCDDA 2014a), as well as monitoring the websites that sell them (Schifano et al 2010), this has resulted in a somewhat 'trainspotter' approach to charting the field. Indeed the European Monitoring Centre for Drugs and Drug Addiction [EMCDDA] annual report graph which charts the new additions to the NPS cornocopaeia each year has become an essential element of NPS conference presentations in this field.

Unsurprisingly, given the wide variations in definitions of NPS, the consequent identification and publication of NPS-related problems and mortality rates themselves have been contentious, highly publicised and highly politicised (King and Nutt, 2014; Goodair et al., 2014). Whilst Cope from the UK Office for National Statistics argued that "there is no official definition of a new psychoactive substance" (2014: 1715), perhaps the closest to a consensus is the EMCDDA definition. Article 3 of EMCDDA Council Decision 2005 defines New Psychoactive Substances as "A new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the 1961 United Nations Single Convention on Narcotic Drugs or the 1971 United Nations Convention on Psychotropic Substances, but which may pose a public health threat comparable to that posed by substances listed in these conventions", a definition which was adapted for use by the UK New Psychoactive Substances Ministerial Review Expert Panel (2014:4). However, this definition of NPS is weakened by the ambiguity of 'new' and the redundancy of 'may pose a public health threat' given that all drugs carry some degree of risk.

The legal conundrum

A notable feature in the evolution of the term has been the reduced emphasis on legal status which leads to the central unanswered question: exactly what is *new* or *novel* about New Psychoactive Substances? A definition which focuses on legal status (eg. ACMD, 2011) is no longer relevant for many contemporary legislative jurisdictions as we have a situation where NPS are rapidly and broadly controlled through 'blanket bans', analogue legislation,

from 2012 onwards. Four high profile deaths over the Christmas 2014 holiday period were attributed to pink 'Superman' tablets sold as ecstasy but which contained a high dose of PMMA (http://www.bbc.co.uk-england-suffolk-30709953). Blue 'Batman' tablets sold in the UK in 2014 were reported to contain a large amount of NBOMe, while other tablets sold as ecstasy were reported to contain methylone or 4-MTA (http://www.independent.co.uk/life-style/health-and-families/features/the-evolution-of-ecstasy-from-mandy-to-superman-the-effects-of-the-drug-mdma-9959732.html)

generic legislation, temporary controls and amendments to existing drug controls.[4] In the UK for example, many NPS are already controlled through generic legislation shortly after or even considerably before they make an appearance and without recourse to established risk assessment processes for individual substances that were previously central to many policy structures but which are now considered too cumbersome in the face of the speed and scale of NPS development. This has led to a cycle of rapid and wide ranging legislative change which is illustrated in the UK's use of generic legislation which prohibits the possession and supply of whole families of drugs without individual risk assessments. The government's NPS Review Expert Panel reported that "over 550 NPS have been controlled since 2009, with 350 controlled since July 2010 … The UK has banned the majority of NPS seen in the EU since 2005. Of the 410 NPS identified in Europe up to 2014 … over 85% of the main groups are already controlled" (2014: 17).

Whilst most of the changes to NPS terminology have resulted in a net widening effect, it is interesting to note that some definitions have resulted in a reduction in the number or scale of drugs covered. As NPS have been controlled, illegal markets have developed and some NPS use has bedded in and become established into the repertoires of drug users and suppliers. Consequently some NPS, most notably mephedrone, are now documented separately to other/all NPS in official reports (eg. Public Health England, 2014).

A definition which centres on the *novel* element overlooks the continuities between pharmaceutical and recreational drug developments in recent years and also the appearance of 'new' drugs and their use by recreational users before, as well as after, 2008. However, as the NPS definition has evolved to include both legal and illegal drugs, so it has come to include "substances that are not necessarily new but which have recently been increasingly abused" (International Narcotics Control Board, 2013: 36). This net-widening has meant that some of the broadest NPS definitions now include:

i. not particularly 'new' illicit drugs (eg. ketamine, GHB/GBL), and in some cases more traditional illicit drugs (eg. psilocybe, khat) whose recreational use has been increasingly noted in some dance club scenes from the 1990s onwards (Measham et al 2001), and

[4] Space constraints preclude a detailed discussion of NPS policy options and implications, which can be found elsewhere (eg. NPS Review Expert Panel, 2014).

including psilocybe and khat products that were sold from 'headshops' prior to their prohibition (2005 and 2014, respectively) in the UK);

ii. a merging of NPS with 'club drugs' or 'dance drugs' (notably ecstasy, cocaine and amphetamines);

iii. long standing uncontrolled psychoactive drugs (eg. nitrous oxide, 'poppers');

iv. medicines which are legally manufactured and prescribed, and which again only recently were recognised as having any recreational appeal. Although 'indirectly' psychoactive (intoxication effects are typically described as 'side effects'), these various medications and pharmaceuticals can also be obtained without prescription from online pharmacy websites, some of which also sell the more popular NPS. These include psychiatric drugs (eg. anti-depressants, anti-psychotics); sleeping pills (eg. chlorals, Z-drugs); analgesics with recently recognised abuse potential (eg. tramadol, pregabalin); and wholly or predominantly physiological drugs, including sexual potency drugs (eg. sildenafil), performance enhancing drugs (notably steroids), cognitive enhancing drugs (eg. modafinil) and image enhancing drugs (such as melanotan and botox).

Significantly, most definitions of NPS exclude the 'new' forms and uses of the three main legally regulated drugs around the world, namely caffeine (eg. caffeine tablets, powder, and even shampoos; high strength 'energy' drinks); alcohol (eg. alcohol powder or 'palcohol', inhalable alcohol vapour); and nicotine (eg. e-cigarettes, shisha, and medicinal nicotine products).

As we can see, the ongoing evolution of terms in the field of NPS studies has blurred what were once considered fairly clear distinctions. In particular – and despite 'legal highs' still being the most commonly used term for NPS in the media and everyday conversation – the legal/illegal distinction causes increasing problems given the national and temporal differences in drug laws, along with the variations implicit in the term 'legal' (notably regarding production, supply and use). Consequently, attempts at precise definition often lead to semantic dances about what NPS are *not*, such as: any psychoactive drugs which are not legally controlled, more particularly meaning *not* legally controlled for medical use, *not* legally prohibited, and *not* licensed for recreational use. Unsurprisingly, a series of alternative terms has emerged, with NPS – which potentially sidesteps the legal/illegal distinction – coming to dominate. The broadest and most flexible definition of the 'new'

prefix of NPS would be: legal or illegal drugs which have been recently discovered, marketed, and/or notably consumed. An operational definition of 'new' could also specify a cut-off year relating to the rise of these 'new drugs' markets, such as the 2008/09 mephedrone 'watershed' in the UK discussed further below, with NPS relating as much to a new *cultural* phenomenon as to specific psychoactive drugs. In this way NPS could be characterised as a flexible collective noun more akin to terms such as 'dance drugs' or 'club drugs' (Coomber et al 2013).

Some colloquial terms for groups of NPS have also been coined by researchers across the globe. The main examples include 'research chemicals' for synthetic NPS (notably hallucinogens); 'herbal highs' for plant-based NPS; 'spice', 'mamba', or 'herbal incense' for synthetic cannabinoids; 'bath salts' for stimulants (particularly for cathinones in North America); and 'smart drugs' or 'nootropics' for eugeroic stimulants (see Table 1 below).

To conclude, our assessment of the evolution of the terms and concepts which describe and demarcate NPS includes consideration of the role of historical and socio-cultural context to this definition. Thus, given the semantic ambiguities and cultural variations of this still developing term, this chapter adopts the following operational definition of NPS: those drugs emerging or rising significantly in use after the 2008 mephedrone 'watershed', starting with first generation synthetic cannabinoids and cathinones, followed by a widening array of substances which are typically uncontrolled to begin with. Drugs controlled and/or whose recreational use was established before 2009 and those in the four categories outlined above are largely absent from the later sections of this chapter unless included in our summaries of other studies that include them.

Classifications of NPS – towards a new taxonomy

In order to review the evidence on NPS - and to design research studies - it is necessary to go beyond the sculpting of clear and precise definitions such as those discussed above, to a principled classification of NPS. Therefore, in this section, we briefly examine the available conceptual frameworks for categorising NPS - that is, models developed to organize and classify specific NPS into broader categories according to rules of inclusion and exclusion. Whilst a variety of classification systems exist in the literature, few are widely accepted

across all disciplines and professional groups involved with NPS, and the constantly evolving nature of NPS means that they can rapidly become outdated. The most common four dimensions of extant classifications are: by source, by legal/medical status, by psychoactive effect (on the brain and mind), and by chemical group. We discuss these four dimensions below before presenting a new multi-level classification of NPS based on two of the most important dimensions.

Source classification

The source classification is relatively straightforward: NPS can be broadly divided into natural and synthetic drugs. Natural NPS can be sub-divided into plant-based drugs (eg. salvia, peyote, amanita muscaria) and animal-derived drugs (eg. cane-toad skin excretions). Plant-based drugs (or plant extracts) are an NPS category frequently used by researchers. Synthetic NPS can be sub-divided into semi-synthetic drugs (production of which starts with a natural drug) and fully synthetic drugs (made without recourse to natural drugs). A third classification by source is 'electronic highs', though these are outside the scope of this chapter (Newcombe, 2012b). Also, as noted above, some NPS products contain a mixture of natural and synthetic drugs: notably 'synthetic cannabis' products, which may contain minor plant-based drugs mixed with synthetic cannabinoids (Uchiyama et al, 2010).

Legal classification

Another common way of classifying NPS is by their legal status, which derives from national legislation assigning controlled drugs to classes/schedules, with criminal penalties for possession and trafficking offences reflecting the level of legal categorisation. This system is not fixed but constantly evolves as new legislation to control emerging NPS is introduced, and as laws in different countries are amended to allow new or revised categorisations. National legislation on drugs, typically enacted in Medicine Acts, also covers medical and non-medical aspects of NPS use and supply (notably regulations on prescribing and dispensing). International legislation derives from the United Nations (notably the three drugs conventions) and in Europe from the European Union (EU) Parliament.

Focusing on the UK, NPS are categorised by the Misuse of Drugs Act 1971 (MoDA) in two ways: by three classes (A to C) which determine the penalties for possession and trafficking offences (up to life imprisonment for trafficking class A drugs); and by five schedules (1 to 5)

which regulate prescribing and dispensing (the strictest being schedule 1, which means the drug has no recognised medical use). Over the 21st century, a growing number of NPS and new/problematic medical drugs have been legally controlled in the UK by successive amendments to the MoDA (see Table 1). [5]

[5] In 2011, the UK MoDA was amended to allow for the passing of a 'temporary class drug order' (TCDO) which bans the sale (but not possession) of a potentially harmful new drug for a period of approximately 12 months to allow an assessment to be made of the need for permanent restrictions on sale and possession. In the first two years, three drugs were placed under a TCDO - methoxetamine, 5/6-APB and NBOMe compounds – all of which were subsequently banned (see Table 1).

Table 1: Drugs controlled in the UK in the 21st century, by amendments to 1971 Misuse of Drugs Act

YEAR	DRUGS	CLASS & SCHEDULE
2001	• 35 phenethylamines	A1
2003	• GHB (gammahydroxybutyrate)	C4i (C2 from 1/15)
2005	• psilocin-based mushrooms (live/fresh) • ketamine	A1 C4i (B3 from 6/14)
2009	• 1ST generation synthetic cannabinoids • GBL (gammabutyrolactone), 14BD (butanediol) • BZP (benzylpiperazine) & other piperazines	B1 C C1
2010	• mephedrone & substituted cathinones	B1
2012	• 2DPMP (desoxypipradol/Ivory Wave) • phenazepam • pipradol esters & ethers (piperidines)	B1 C2 C3
2013	• 2nd generation synthetic cannabinoids • methoxetamine – desmethyltramadol • lisdexamphetamine • zopiclone & zaleplon	B1 B1 B1 B2 C4i
2014	• NBOMe compounds • benzofuran compounds (5-APB, 6-APB) • khat • tramadol	A1 B1 C1 C3
2015	• dimethylaminorex (4,4'-DMAR) • cyclohexyldiphenylethylpiperazine (MT-45) • tryptamine compounds (AMT, 5-MeO-DALT) • lysergamides: ALD-52, ETH-LAD, PRO-LAD, AL-LAD, LSZ • AH-7921 (opioid) **Planned** • 3rd generation synthetic cannabinoids • psychoactive Substances Bill proposing 'blanket ban' on sale of all psychoactive substances with some exemptions • possible ban on all drugs affecting CB1 brain receptor **Reclassification and rescheduling** 2004 cannabis C1 (from B1) 2007 methamphetamine A2 (from B2) 2009 cannabis B1 (from C1) - except Sativex (B4i) 2014 ketamine B2 (from C4i) 2015 GHB C2 (from C4i)	A1 A1 A1 A1 A1 A1

Psychopharmacological classification

Perhaps the most common ways of classifying NPS are by their psychoactive effects and chemical groups, including their impact on neurotransmission. The taxonomy of NPS presented here was influenced by several sources including drug definition and classification schemes used on such websites as Wikipedia and Erowid, along with models implicitly or explicitly identified by researchers, trainers and organizations (EMCDDA, 2014a; Dargan & Wood, 2013; Mentor-Adepis, 2014; Zohara et al., 2014).[6] Adley's Drug Wheel is particularly useful, combining seven categories of broad psychoactive effect - depressants, opioids, stimulants, cannabinoids, empathogens, psychedelics and dissociatives – with a two-way classification by legal status in the UK (http://thedrugswheel.com/). By April 2015 it covered 100 drugs/drug groups, including 69 controlled substances and 31 non controlled substances. Its main limitations are the relevance of its legal classification to the UK only and its basis in just one psycho-chemical classification level.

In our proposed classification of NPS, psychoactive drugs can be organised according to a conceptual framework founded on two primary orthogonal dimensions of altered brain activity: stimulant-depressant and hallucinogenic-antipsychotic. However, with the notable exception of cannabidiol, there are very few psychoactive substances with predominantly anti-psychotic effects in common use. Accordingly, our scheme bases the first categorisation level (general effect on the CNS) on the tripartite distinction between depressants, stimulants and hallucinogens. The second level categorises NPS into nine families of psychoactive effect, namely: inebriant, sedative and analgesic families of depressants; euphoriant, eugeroic and entactogen families of stimulants; and psychedelic, dissociative and deliriant families of hallucinogens. The third level categorises NPS into 37 chemical groups, and the fourth category itemises the hundreds of drugs which come under these

[6] Recent reviews of the evidence about particular categories of NPS include: amphetamines (Lapoint et al. 2013); cannabinoids (ACMD 2014, Auwarter et al. 2013, Kickman & King 2014, Linnell 2014); piperazines (Gee & Schep 2013); cathinones (ACMD 2010, Wood & Dargan 2013); pipradols (White & Archer 2013); aminoindanes (Brandt et al, 2013); arylcyclohexylamines (Chan et al, 2013, Greene 2013); phenethlyamines (King 2013); benzofurans (Greene 2013); dimethoxyphenethylamines/NBOMe (ACMD 2013); and tryptamines (ACMD 2014, Greene 2013).

headings[7] - these can be further divided into legal and illegal drugs according to national laws. It should be noted that there are many types and levels of chemical classification and the categories used in Table 2 are open to further refinement.[8]

Table 2 presents the taxonomy of drugs considered to be NPS according to at least some of the many definitions discussed above, which cover both 'new' drugs and 'legal' drugs, as well as drugs available from High Street 'headshops', online websites and other sources in the case of drugs such as laughing gas, poppers, khat and magic mushrooms. The scheme can also be modified and tightened to focus on NPS by our earlier operational definition (at the levels of chemical group and specific drugs). Clearly, given that the effects of drugs vary widely by sub-types and consumption patterns (eg. route of use, dose, setting), some drugs or drug categories could arguably be classified under alternative headings. For instance, the entactogen family could be included under the class of hallucinogens or stimulants, because entactogens vary widely in their effects and when consumed in different ways. Similar considerations apply to cannabinoids Even so, our taxonomy provides a useful framework for understanding and discussing NPS and will be used to organise the evidence which follows.

[7] Specific chemicals sold as NPS branded products are also given trade names by manufacturers and retailers but these are not used here.

[8] Space constraints preclude a more detailed discussion here. More detailed definitions of these classes of drugs, covering their chemistry and psychopharmacology, can be found on such websites as Erowid and Wikipedia.

Table 2: A new taxonomy of New Psychoactive Substances

Psychoactive Effect		**Chemical Classification**	
Class	*Family*	*Group*	*Specific NPS*
Depressant	Sedative	• Benzodiazepine	*phenazepam, etizolam, brotizolam*
		• Anti-histamine	*diphenhydramine, promethazine, cyclizine*
		• GHB-type	*GHB, GBL, GBK, 14BD*
		• Kavalactones	*methysticin, yangonin, kavain [kava: 15]*
		• Z-drugs	*zopiclone, zaleplon*
	Analgesic	• Opioid	*MT-45, AH-7921, doxylam, carfentanil, ocfentanil*
		• Kratom compound	*mitragynine, hydroxymitragynine*
Stimulant	Euphoriant	• Amphetamine	*fluoroamphetamine, 4-methylamphetamine*
		• Cocaine analogue	*dimethocaine, fluorotropacocaine*
		• Cathinone - natural	*cathinone, cathine [khat]*
		• Pyrrolidine	*naphyrone, pyrovalerone, MDPV*
		• Piperazine	*BZP, TFMPP, mCPP, MeOPP*
		• Piperidine	*pipradol, 2DPMP, DPMP,*
		• Oxazoline	*ethylphenidate*
		• Aliphatic amine	*methylaminorex, dimethylaminorex (DMAR)*
			dimethylamylamine (geranamine)
	Eugeroic	• Pyridine	*nicotine, arecoline, cotinine, cytisine*
		• Xanthine	*caffeine, theobromine/theophylline*
		• Benzhydril-sulfinyl	*modafinil, armodafinil, adrafinil*
		• Ephedrine	*ephedrine, pseudo-ephedrine, cathine*
	Entactogen	• Phenethylamine	*25B-NBOMe, 25I-NBOMe, bk-2CB, mescaline*
		• Cathinone - synthetic	*mephedrone (m-cat), methylone, methedrone*
		• Aminoindane	*MDAI, MMAI, 5-IAI, 2-AI, TAI, ETAI*
		• Benzofuran	*5/6-APB, bromo-dragon FLY, 2C-B-FLY*
Hallucinogen	Psychedelic	• Lysergamide	*LSA, LSH [ipomea]*
		• Tryptamine	*AMT, AET, 5-MeO-DALT, 4-HO-MET*
		• Cannabinoid (SCRA)	*JWH-018, AM-2201, CP-47, 5F-AKB-48, XLR-11*
		• Harmala alkaloid	*harmaline, harmine (beta-carbolines)*
	Dissociative	• Arylcyclohexylamine	*methoxetamine, dephenidine, tiletamine*
		• Other NMDA-RA	*nitrous oxide, dextromethorphan*
		• Diterpenoid	*salvinorin-A [salvia]*
		• Isoxazole	*muscimol, ibotenic acid [amanita]*
	Deliriant	• Alkyl nitrite	*amyl nitrite, butyl nitrite, isopropyl nitrite*
		• Anti-cholinergic	

	• Hydrocarbon • Haloalkane	*atropine, scopolamine, hyoscyamine* *toluene, butane, petroleum* *chloroform, chlorofluorocarbons (CFCs)*

KEY

NMDARA: N-methyl-D-aspartic acid receptor antagonist

SCRA: synthetic cannabinoid receptor agonist

[ ] = plant source

Trends in NPS production, supply and use

This section provides a brief overview of the main evidence concerning the development of NPS markets, including trends in production, distribution, availability, prevalence of use and consumption.

The challenges of defining and measuring drug use in general have been widely discussed elsewhere in this collection, and in relation specifically to NPS here. These ongoing challenges make estimating the prevalence of use – across drugs and population groups – even more complex. Moreover, allowing for the usual caveats for drug prevalence research (Newcombe, 2007), NPS research is even more challenging because of the large numbers of substances, their rapid development and changing legal status, and the complexities of identifying and matching chemical compounds with branded retail products and the street or slang names adopted by different user groups. The lists of actual and potential drugs cast an increasingly gloomy shadow across research on patterns and prevalence of NPS use. This has led some researchers (including one of the authors) to embrace greater cross disciplinary collaboration and triangulation in order to explore what users have bought and believe they are consuming by comparison with what retailers have bought from manufacturers and believe they are selling - resulting in fertile collaborations between criminologists, chemists and toxicologists (eg. Archer et al., 2014a, b). Whilst urine testing as a validation tool for self reported drug use is nothing new (eg. Measham et al., 2001), the scale of mass pooled urine analysis in recent years across Europe (EMCDDA ,2014b) in large part has been fuelled by the rapid expansion in the number of NPS and the need to ascertain their prevalence of use whilst challenging the constraints of traditional self report data collection.

Global NPS use

The World Drug Report (UNODC 2014: 51) has reported that NPS use is now “a truly global phenomenon”. Of 103 countries on which relevant information was available in December 2013, 94 reported the emergence of NPS markets, up from 70 out of 80 at mid-2012. The total global number of NPS has more than doubled from 166 in 2009 to 348 at the end of 2013 (including 97 NPS identified for the first time in 2013). This has led to the unprecedented situation of “the number of NPS clearly exceed[ing] the number of psychoactive substances controlled at the international level” (UNODC 2014: 52): that is,

348 NPS compared with 234 controlled drugs. The main drug groups comprising the 348 NPS included cannabinoids (29%), phenethlyamines (21%), cathinones (15%), tryptamines (8%), plant-based drugs (6%), piperazines (4%), arylcyclohexylamines (3%), aminoindanes (1%), and other NPS groups (11%).

The Global Drug Survey (GDS) accesses predominantly young adults through a range of general and specialist media websites such as The Guardian, Fox News and Mixmag. The 2013 GDS was based on a self selecting convenience sample of 78,800 people (Winstock, 2014). Across the 18 countries with sample sizes of over 600 (average sample size: 4,000), 12% reported having used NPS/'legal highs' in the last year (using a broad definition of NPS which includes longstanding and non synthetic psychoactive substances including nitrous oxide and salvia) and 22% reported having bought drugs online. Of the ten types of NPS use reported, last year use of nitrous oxide was the most common (6%), reported by 14 countries and ranging from 1% in Portugal to 27% in the Netherlands. The other two most popular NPS were salvia and synthetic cannabinoids, with national rates of use ranging from 1% to 10%. The report on the December 2014 GDS noted that there was a substantial drop in last year NPS use to 7% (Winstock, 2014). Among the 11 countries with over 1,500 respondents, last year use of NPS varied from below 10% in nine countries to 12% in the UK. Overall, the most commonly reported 'research chemicals and legal highs' were synthetic cannabinoids: 2% reporting having used them in the last year.

A review of the literature on the epidemiology of NPS use by Sumnall and colleagues concluded that aside from mephedrone, salvia divinorum and SCRAs "most other NPS appear not to have made a significant impact on the drug market with respect to use preference … [and] remain infrequent choices" (2013: 99). They note that "most data on NPS epidemiology comes from (small) convenience samples", which produce findings with limitations given that "such data can only reveal drug use behaviours in the respondents surveyed, and cannot easily be generalized beyond the study" (2013: 99). Although the authors did not mention that nitrous oxide use is second only to cannabis in the UK and is the most popular NPS in the UK general population survey (Home Office, 2014), this may be because nitrous oxide only recently was included in (some) definitions of NPS.

USA

The US office of National Drug Control Policy (2014) reported that the number of new synthetic drugs identified in 2012 reached a record 158, including 51 cannabinoids (compared with two in 2009), 31 cathinones (compared with four in 2009), and 76 other new drugs. The number of hospital emergency department visits involving synthetic cannabinoids more than doubled from 11,406 in 2010 to 28,531 in 2011 (Substance Abuse and Mental Health Services Administration, 2013).

Indeed, research consistently indicates that synthetic cannabinoids are the most popular type of NPS in the USA, although it should be noted that this depends on how NPS are (or are not) defined and classified, including which NPS are itemized in survey questionnaires and which NPS are included under standard drug group headings in surveys. For instance, the Monitoring the Future (MtF) self report annual surveys of US college students and young adults, based on repeated cross sectional surveys of high school graduates, have been reported from 1976 to 2013 (Johnston et al., 2014b). The MtF surveys of over 40,000 secondary school students and several thousand college students and young adults aged 19 to 28 years has reported the prevalence of last year use of three itemized NPS in recent years (see Table 3) (Johnston et al., 2014a,b). However, it is likely that drugs classified as NPS in some other studies or reporting systems are incorporated under general drug group headings in the MtF study – including hallucinogens (eg. NBOMe), inhalants (eg. nitrous oxide), tranquillizers (eg. phenazepam) and opioids (eg. MT-45).

Table 3: NPS use among 8th to 10th graders in US secondary schools, and college students and young adults, 2009 to 2014

	Synthetic cannabis					**Synthetic stimulants**					**Salvia divinorum**				
	8th	10th	12th	CS	YA	8th	10th	12th	CS	YA	8th	10th	12th	CS	YA
2009													5.7	5.8	3.5
2010											1.7	3.7	5.5	3.5	3.6
2011			11.4	8.5	7.4						1.6	3.9	5.9	3.1	2.2
2012	4.4	8.8	11.3	5.3	5.3	0.8	0.6	1.3	0.3	0.5	1.4	2.5	4.4	1.5	1.5
2013	4.0	7.4	7.9	2.3	3.2	1.0	0.9	0.9	0.1	0.4	1.2	2.3	3.4	1.0	0.9
2014	3.3	5.4	5.8			0.5	0.9	0.9			0.6	1.8	1.8		

CS: college students
YA: young adults (19-28 years)

In 2014, levels of last year use of synthetic cannabinoids (also referred to as 'K2/Spice') ranged from over 3% among 8th graders to almost 6% among 12th graders. These represent significant drops from the previous year, and levels for all three grades have dropped steadily since 2012. Levels of last year use of salvia also dropped two to three-fold from 2010 to 2014 to below 2%, and last year use of synthetic stimulants ('bath salts') was reported by fewer than 1% of students in all grades in 2014. Levels of last year use of all three NPS have fallen fairly steadily across recent years for both groups, and to lower levels than those for school students by 2013 – 3% or lower for cannabinoid use, and 1% or lower for use of salvia and stimulants.

Prevalence of NPS use across Europe

The Early Warning System run by EMCDDA (2015) reported that more than 450 NPS were currently being monitored across the EU. Overall 299 different NPS were detected in 2013: 101 newly identified and 198 previously identified NPS. The most commonly identified types since 2008 were synthetic cannabinoids (134) and cathinones (77). NPS identified for the first time reached a record 101 in 2014, compared with 81 in 2013, 74 in 2012, 49 in 2011, 41 in 2010, 24 in 2009, and 13 in 2008. The most common new types identified over the last two years were: cathinones (from 7 in 2013 to 31 in 2014), cannabinoids (from 29 to 30), phenethlyamines (from 14 to 9), arylalkylamines (from 7 to 4), opioids (from 5 to 5), tryptamines (from 1 to 5), benzodiazepines (from 2 to 4), and other synthetic substances (from 16 to 13).

Seizure figures for 2013 show that there were a record 46,370 seizures of over 3.1 tonnes of NPS, with the two main types including 21,495 seizures of almost 1.6 tonnes of synthetic cannabinoids, and 10,657 seizures of more than 1.1 tonnes of synthetic cathinones. There was a seven-fold increase in reported NPS seizures between 2008 and 2013.

The EMCDDA (2013) identified 651 shops that sold NPS as 'legal high' products or 'research chemicals', a slight decrease on 693 in January 2012, but higher than the 631 in July 2011, 314 in January 2011, and 170 in 2010. The July 2011 snapshot exercise found that the three NPS most commonly sold by the online shops at that time were all plant products: kratom (128), salvia (110), and hallucinogenic mushrooms (72). The next three most commonly sold NPS were synthetic drugs: MDAI (61), methoxetamine (58) and 6-APB (49) (EMCDDA 2011a, b). The UK was home to 121 of the shops.

The European Commission 'Flash Eurobarometer' survey of 'young people and drugs' was based on telephone interviews with over 13,000 15 to 24 year olds in all 28 EU Member States in June 2013. The average EU figure for reported lifetime use of NPS increased from 5% in the 2011 survey to 8% in the 2014 survey (EC 2014). The top six countries for NPS use all exhibited increases in lifetime use of NPS from 2011 to 2014: Ireland (from 16% to 22%), Slovenia (from 7% to 13 %), Slovakia (from 7% to 13%), Spain (from 5% to 13%), France (from 5% to 12%), and UK (from 2% to 10%). The biggest increase was in the UK, where the proportion of NPS users increased fivefold between the two surveys.

NPS availability and use in the UK

Official statistics

Though national NPS seizure figures are not available, the number of seizures of NPS in prisons in England and Wales has been reported to have increased significantly, from 16 in 2010, 90 in 2011, 138 in 2012, 267 in 2013, and 436 in the first 7 months of 2014 (Parliamentary Question, September 2014). Each year, the vast majority of these seizures involved synthetic cannabinoids (from 15 in 2010 to 430 in the first half of 2014), and the prison authorities have reported that use of these NPS leads to increased violence and disorder among inmates. A qualitative study of NPS that included interviews with prisoners and ex-prisoners also reported that synthetic cannabinoids are the most popular drug in UK prisons (Linnell et al, 2015).

The 2013/14 annual report of the UK Forensic Early Warning System (FEWS) noted that "so far the Coalition Government has controlled over 350 NPS, by group or generic definitions,

including some not seen in the UK, under the 1971 Act" (FEWS, 2014: 4).[9] The total number identified since 2011 was 31, including 10 cannabinoids, four tryptamines, three phenethlyamines, and three cathinones. Analysis of NPS samples collected by FEWS found that around nine out of ten were mixtures of either two (61%) or three (30%) active drug ingredients. In 2013/14, 3% of internet and 4% of headshop samples contained controlled NPS, compared to 16% and 64% in 2012/13. However, 88% of festival samples contained controlled drugs in 2013/14, a similar amount to 2012/13 (84%) (FEWS, 2014).

An NPS was the primary drug[10] of concern for 144 people in drug treatment in England in 2013/14 – just under 0.1% of all drug treatment clients (Public Health England, 2014). However, separate statistics for mephedrone and GHB/GBL indicated that the number of NPS users in treatment had almost tripled over the last three years.

General household surveys

Annual general household surveys of drug use are conducted in all countries of the UK but due to space constraints, we focus here on prevalence surveys in England and Wales only (see UK Drug Focal Point, 2014, for a summary of NPS use across the UK). The annual Crime Survey for England and Wales (CSEW) includes a general household survey of drug use among over 20,000 adults (Home Office, 2014) and is the most robust national data set on drug prevalence in the UK. Over the six years ending 2014/15, the CSEW has reported on the prevalence of use of seven types of NPS: mephedrone, spice, khat, BZP, GHB/GBL, nitrous oxide and salvia. Overall lifetime and last year use of mephedrone has declined steadily for both adults and young adults since it was controlled and national data was first collected in 2010, although it rose slightly in 2013/14 (see Table 4).[11]

[9] Examples of NPS seen in the UK market in the past year are: AKB-48 (a synthetic cannabinoid), 25-B-NBOMe (a phenethylamine) and 4-MeO-PCP (a dissociative anaesthetic) as well as substances sold under branded names such as CRITICAL HAZE (containing 5F-AKB-48), SPARKLEE (containing MPA, 5-MeO-DALT, and 2-aminoindane) and Black Mamba (containing AM-2201, 5-MeO-DALT and JWH-081)" (FEWS 2014: 4).

[10] Primary use of NPS is defined by the National Drug Treatment Monitoring System (NDTMS) for England as drug use which meets these two conditions: (i) no use of opiates or crack in the treatment journey; and (ii) report of primary drug in the earliest episode of the latest treatment journey to cross the reporting year, in any of the following NPS categories: predominantly stimulant, hallucinogenic, dissociative, sedative/opioid or cannabis; or not otherwise specified (Public Health England 2014).

[11] Based on these figures, the total number of lifetime users of mephedrone was estimated to have climbed from 584,000 in 2012/13 to 764,000 in 2013/14; while the total number of last year users climbed from

Table 4: Prevalence of use of mephedrone in England & Wales, 2010/11 to 2014/15 (CSEW)

	ADULTS 16-59		**YOUNG ADULTS 16-24**	
	Lifetime	*Last Year*	*Lifetime*	*Last Year*
2010/11	-	1.3	-	4.4
2011/12	-	1.0	-	3.3
2012/13	1.9	0.5	4.5	1.6
2013/14	2.3	0.6	6.3	1.9
2014/15	2.2	0.5	5.3	1.9

Nitrous oxide and **salvia divinorum**

Both nitrous oxide and salvia remained uncontrolled drugs in the UK at the end of 2014 and therefore although not included in many post-2008 definitions of NPS given their longstanding if low level recreational usage, they are considered to be 'legal highs' by some commentators based on their legal status, effects and availability (to date) from online retailers and headshops. Between 2012/13 and 2013/14, there were increases in the last year use of both of these drugs, for both adults and young adults, with the change in last year use of salvia among all adults being statistically significant (Table 5). Nitrous oxide was the second most commonly used drug by young adults in the UK after cannabis, and the third most commonly used drug by all adults after cannabis and cocaine.[12] The figures on last year use also show that mephedrone and salvia are the fifth and sixth most popular drugs among young adults (ecstasy is fourth).

Table 5: Prevalence of last year use of salvia and nitrous oxide in England & Wales, 2012/13 to 2013/14 (CSEW, Home Office 2014)

	ADULTS 16-59	**YOUNG ADULTS 16-24**

161,000 to 205,000. By 2013/14, these numbers included 394,000 young adults who had ever used mephedrone and 117,000 young adults who had used mephedrone in the last year (Lader 2015).

[12] It can be extrapolated from these figures that the number of last year users of nitrous oxide in the UK climbed from over half a million in 2012/13 to nearly three quarters of a million in 2013/14.

	Salvia	*Nitrous Oxide*	*Salvia*	*Nitrous Oxide*
2012/13	0.3	2.0	1.1	6.1
2013/14	0.5	2.3	1.8	7.6

The CSEW also reported on last year use of four other drugs between 2009/10 and 2011/12 which are included in some definitions of NPS. Last year use of 'spice' and BZP both fell from around half a per cent to 0.1%, while last year use of khat and GHB/GBL remained level at about 0.2% and 0.1% respectively. Between 2009/10 and 2010/11, notable drops in last year use of all four of these NPS were evident among 16-24 year olds, with 25-59 year olds exhibiting stable and lower levels of use. In short, of seven types of NPS assessed by the CSEW, three were fairly popular compared with controlled drugs, while four were used by fewer than 0.2% according to the latest figures available.

Motivations and user groups

In this final section we draw together some of the evidence discussed above to piece together why the NPS phenomenon shot into the spotlight from 2008 onwards and what might be the motivations of users, which then sheds light on who are the key user groups. Whilst many of the reasons for taking NPS are similar to the motivations for consuming a whole host of other psychoactive substances – legal, illegal or prescription; prohibited, controlled or licensed – it is only through an understanding of the inter relationship between established and 'new' psychoactive substances that we can more fully understand their appearance and appeal.

(1) Purity

A key reason for the emergence of NPS relates to their *relative* purity, by comparison with established drugs across Europe in that particular historical period (Measham, 2013). Forensic analyses of ecstasy and cocaine seizures and submissions to drug checking organisations (such as the Dutch Drug Information and Monitoring System or DIMS) in 2008/10 concur that purity was at its lowest level across Europe just before mephedrone became a concern. In the UK for example, purity levels fell to an all-time low for most established controlled drugs in around 2009. Cocaine purity reached a low point of 20% in

2008 (Table 6) and the MDMA content of ecstasy pills fell to a low point of 20mg in 2009 (UK Focal Point 2014), after the emergence of MDMA crystal (MD, Molly) as a higher priced, higher purity 'premium' product in the mid 2000s in the UK (Smith et al., 2009). Conversely, forensic analyses of mephedrone showed that it was being sold at approximately 95% purity before legislative control in 2008-10 (Miserez et al., 2014). Whilst it could be argued that it was merely coincidence that the purity levels of the most popular established illegal stimulants were at their lowest point in decades at the very same time that mephedrone (a legal stimulant with not dissimilar effects to cocaine and ecstasy) first became a concern, studies with users endorse this connection. Interviews with mephedrone users before legislative control in the UK (Measham et al., 2010) articulate a clear narrative of disillusionment with Class A drugs by both recreational drug users and Problem Drug Users:

> *"I guess it has kind of replaced my desire for ecstasy… because I don't really feel like I can get hold of proper ecstasy. Whereas mephedrone I feel much more comfortable taking because I kind of know what I am getting. So in that way it has probably replaced my, yes I would say it probably has – until I can find, if I find a good source of MDMA – it has replaced my use of that drug." (Professional male, 34, 2009, in Measham et al., 2010)*

From 2011 onwards both DIMS and UK forensic analyses suggest that the purity of cocaine and ecstasy increased again across Europe, with the MDMA content of seized ecstasy pills increasing five fold from 20mg to 100mg in the six year period 2008-2014 (ACMD 2015). Conversely, after legislative control of substituted cathinones in 2010, forensic analyses of second generation NPS show that unlike the first generation NPS of high purity, these second generation NPS were of variable content and sometimes even illegal (Brandt et al., 2010). The variable content, effects and legal status of these NPS were widely publicised, capitalised on by politicians and drugs prevention campaigns. This may have dampened some of the initial demand for NPS and resulted in a fall in NPS prevalence rates in annual surveys, including both the general household survey and convenience sample surveys of festival-goers (Measham, 2013) and club-goers (Wood et al., 2012a). The rise and fall in self reported mephedrone use contrasts with the disillusionment and then reinforcement of ecstasy's appeal as the MDMA content of tablets rose to and surpassed their previous levels (Pidd, 2014). So a key point here is that the appeal of NPS products when they first

appeared related to the purity and reliability of their contents *relative* to the purity and reliability of established illegal drugs, and the relationship between the two.[13]

Table 6: Domestic resale mean percentage purity of certain drugs seized by police in England and Wales, 2003 to 2013

	2003	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**
Amphetamines	11	9	10	11	11	8	8	8	10	5	7
Cocaine powder	51	42	43	35	33	29	20	24	26	37	38
Crack cocaine	70	64	65	50	52	43	27	31	26	30	36
Heroin (brown)	33	40	47	44	50	43	44	35	18	20	33
Ecstasy *	65	67	66	48	52	33	44	49	71	102	n/a

- * mg of MDMA base per tablet
- Source: UK Focal Point (2014)

It should not be assumed that there was simple displacement from low purity Class A drugs to high purity legal NPS in 2008/9, however. Annual surveys conducted with club-goers at South London gay-friendly dance clubs from 2010 onwards have shown consistently high levels of self reported mephedrone use each year, with mephedrone becoming the drug most likely to be consumed on a night out and also these club-goers' favourite drug (Measham et al 2011a; Wood et al 2012b). However, these surveys found no evidence of wholesale displacement from Class A drugs such as cocaine and ecstasy to NPS, but rather mephedrone appeared to have been added to existing drug-using repertoires and was being used as a supplement, a secondary drug, to 'top up' low purity Class As (Moore et al., 2013). This is supported by the general population survey (Smith and Flatley, 2011) which reports that nine in ten mephedrone users reported having used other illegal drugs in the last year. These various studies suggest, therefore, that purity was a particular appeal for users who were already experienced Class A drug users, such as club-goers. A further indicator of the elasticity of demand for mephedrone and its possible status as a 'topping up' drug relates to

[13] There is some evidence that purity levels and accurate labelling is increasing again amongst third generation NPS products (FEWS 2014; ACMD 2015).

the fact that the price only rose to £20/25/gram after legislative control in 2010 and has stayed at that price since then.[14]

(2) Availability

This has been a significant driver to NPS use: for the first time psychoactive drugs were widely, cheaply and legally available online, in specialist headshops, market stalls, festivals and (of increasing concern) at small independent convenience stores and petrol garages with variable retail practices (NPS Review Expert Panel, 2014). However, as with purity, availability of NPS is also *relative* and usually gauged in comparison with the access and availability of illegal drugs. So for users who either could not access or did not want access to established drugs through street 'dealers', legal NPS hold an obvious appeal.

The DrugScope 2013 street drug trends survey, based on information from drugs workers at 25 agencies in mainland Britain, revealed that the main source of NPS was not internet websites but specialist 'headshops' and also non-specialist shops such as petrol stations, pet shops, takeaway food shops, newsagents, tobacconists, sex shops and market stalls. While few young people were coming forward to treatment services, outreach workers reported that some young people were at risk of serious health consequences, a finding confirmed in the qualitative study by Linnell and colleagues (2015). Daly (2013) also reported that a snapshot survey carried out in Newcastle of 116 people (mainly teenagers aged 16–17) found that, of those who had recently bought 'legal highs', 45 had purchased them from headshops, while 20 had bought them from a petrol station or takeaway food shop.

Availability of NPS appeals particularly to teenagers and novice users without established contact with illicit subcultures and illegal economies (evidenced in the disproportionate numbers of patients in their mid teens hospitalised for SC-related problems in the UK). Others who may not be able to access illegal drugs through street dealers may be residents in rural areas without easy access to urban street markets and middle class professionals who were suddenly able to order NPS products online with a credit card and without the risks associated with purchasing illegal drugs such as being exploited by street dealers or caught by the police. The converse of this is that once mephedrone was banned self reported use fell (eg. Lader, 2015; Measham, 2013, Winstock, 2014) suggesting that at least

[14] Whilst it doubled in price compared with its legal price of £10/gram, it remains at about half the price per gram of MDMA and cocaine in the UK.

in part, once availability plummeted, so did use. Furthermore, for those who continued to use controlled NPS, their use was likely to be more risky in terms of both physical and social harms due to greater variations in content and purity in unregulated markets combined with accessing criminal supply networks.

(3) Legality

If prevalence of NPS use falls in the years after legislative control, as indicated with falling mephedrone use in the UK general household survey discussed above (Lader 2015), then perhaps this can be seen as evidence of a deterrent effect of banning drugs, as distinct from the impact of reduced availability resulting from the ban on legal sales? In general there is a weak evidence base on the deterrent value of criminal law. What we know from international comparative drug policy analyses (eg. EMCDDA, 2011c; Stevens, 2011) and regional times-series data (eg. Wood et al., 2012b) is that there appears to be little impact of drug policy change on drug use in a range of different jurisdictions.

Furthermore, in surveys and interviews, users themselves rarely prioritise legal status when discussing why, or indeed why not, to take illegal drugs (eg. Parker et al., 1998). Research with users has found that more important reasons for taking or avoiding drugs include price, purity, availability, perceived pleasurable/unpleasant effects, curiosity and the wider social context to use (Norman et al., 2014; O'Brien et al., 2015). Moreover, if, as discussed above, NPS users are more likely to be experienced drug users and take NPS along with illegal drugs in weekend polydrug repertoires, then the legal status of NPS in particular is of little relevance.

Where legal status has been found to result in a significant appeal for uncontrolled NPS has been for those who come into contact with drug testing, through employers, treatment services, the operation of motor vehicles, and the criminal justice system more generally. For example, SCRAs have been found to hold a particular appeal amongst US professionals (Perrone et al., 2013); UK professionals (Sumnall et al., 2016); UK prisoners (Brown, 2014); UK ex-offenders (Linnell et al 2015) and clients in treatment who are drug tested.

(4) Media

A fourth key driver to NPS use has been the media. Intense media scrutiny of NPS drug-related deaths and NPS policy have led to a symbiotic relationship between press coverage,

policy makers and user demand for drugs (Forsyth, 2012; Measham et al., 2011b). For NPS at least as much as for any other drug problem, there is a sharp contrast between the lack of information regarding short and long term effects of use, the spiralling numbers of psychoactive substances available and the burgeoning easy access both to information and to retailers themselves through the internet. Although not unique to NPS – the early internet was utilised when ecstasy gained popularity with 1990s dance club cultures[15] – it has been widely noted how pivotal the internet has been to the development of NPS (Forsyth, 2012; Schifano et al., 2010), with NPS being considered the first group of drugs to be born out of the internet age. Indeed the internet has played a multi faceted role in relation to the development of NPS, from the facilitation of multi media news, research data collection and dissemination, dark and clear net retail outlets, to online user forums and virtual communities (Barratt et al 2014; O'Brien et al., 2015).

Conclusion: From 'cat and mouse' to 'hare and hounds'

In answer to the question what is new about New Psychoactive Substances, it is the speed of innovation combined with the globalisation and virtualisation of drug markets and user groups that have together led to the essential 'newness' of the NPS phenomenon. However, within this innovation also lies another key feature of the NPS debate. The rapidity of NPS manufacturing and marketing innovations move in conjunction with the rapidity of policy developments. This relationship between pharmacological and policy developments was widely characterised in the early years as a 'cat and mouse' relationship (including by the authors elsewhere: Measham et al., 2010), with NPS chemists and entrepreneurs ready to respond to each new piece of legislation. Having seen several generations of NPS and NPS-related legislation now develop, one of the authors[16] has suggested that it is perhaps more accurate to characterise this relationship between NPS development and policy change as 'hare and hounds' rather than 'cat and mouse' because it is the speed of policy change which itself is the driving force behind the faster and faster pace of NPS innovations. Without each set of generic controls of SCRA in the UK, for example, it is highly unlikely that

[15] With ecstasy came the advent of ecstasy information and analysis forums and pill report sites eg. www.ecstasy.org.

[16] Measham, F (2014), The Unfathomable Foggyiness of Being: User motivations, market practises & policy implications, presentation to NPS conference, Queen Mary College, London, May 2014.

there would have been a further generation of SCRA development within such rapid succession of the previous one.

In conclusion, we see pockets of popularity and differentiated demand for NPS around the world, with legislative control impacting on purity, availability, price and appeal for some drugs in some areas, but persistent use by some others. Although prevalence of use of NPS remains low by comparison with established illegal drugs in most countries, the significance of the rise of 'legal highs' relates to the rapidity of innovation in this area and also the speed and scale of policy responses. In contrast to established illegal drugs, control regimes have been quick to respond to the perceived threat, the level of which has led to innovation and expansion of control regimes. Therefore rather than a 'consensus fracture' as we have seen in relation to established illegal drugs and the 'war on drugs' (Bewley-Taylor, 2012), global drug prohibition regimes have indicated their capacity for innovation, adaptation and co-operation, with a tightening of the drug policy ratchet and the blanket of prohibition being thrown wider (Stevens and Measham, 2014). Indeed it is in the response to criticism of prohibition as a creaky structure ill fitted to tackling the emergent NPS problem, that we have seen a reinvigoration, expansion and U-turn away from more liberal regimes with the introduction of the current regime of analogue, generic and 'blanket ban' control measures from 2009 onwards, resulting in a new era for both pharmacological and policy developments.

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